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(54) Title: GELLAN GUM TABLET COATING			
(57) Abstract			
<p>A tablet coating comprising gellan gum is disclosed along with a process which comprises admixing gellan gum and water under effective shear conditions to prepare an aqueous gellan gum coating composition thereof whereby the aqueous gellan gum coating composition is applied in an adherent fashion to a placebo or a tablet containing a pharmaceutical to form a gellan gum coated placebo or gellan gum coated active drug.</p>			

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GELLAN GUM TABLET COATING

FIELD OF THE INVENTION

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This invention relates generally to tablet coatings and to a method to prepare compositions useful to coat tablets. More particularly this invention relates to a tablet coated with gellan gum, use of gellan gum as a coating, a method to prepare a gellan gum composition useful to coat tablets, a gellan gum composition useful to coat tablet(s), and to a method for coating tablet(s) with gellan gum.

BACKGROUND OF THE INVENTION

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Tablets are typically used to deliver a pharmacologically effective amount of a therapeutic drug to humans and animals so as to provide medicinal benefit to the human or animal. Typically such therapeutically effective drugs include those drugs that possess and produce desirable drug effects after effective consumption by the human or animal.

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In medicinal uses, one or more coatings is desired on a medicinal tablet in order to obtain one or more of gloss, better appearance, identification, mouthfeel, stability, color, swallowability, improved taste and the like.

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Many medicinal tablet coatings today are low viscosity hydroxypropylmethylcellulose (HPMC). Usually a HPMC solution of about 10% weight with a viscosity below 1000 cps. (centipoise), with appropriate plasticizer, is applied by a spraying system or device to a tablet in a coating process.

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Even with the foregoing and other tablet coating compositions, the industry continues to desire a product which provides enhanced tablet coating properties. The industry has recognized the need for an improved tablet coating which would provide increased gloss, better mouthfeel at coating quantities at lower levels than conventionally accepted methods, for example. The process of preparing such an improved tablet coating economically and efficiently continues to be of interest.

OBJECTS OF THE INVENTION

10 It is an objective of this invention to provide a tablet coating comprising gellan gum.

15 It is another objective of this invention to provide a tablet coated with gellan gum.

It is an additional objective of this invention to provide a process for preparing a gellan gum composition useful for coating tablets.

20 It is yet another objective of this invention to provide a process for preparing a coated tablet such as a coated placebo or a coated pharmaceutical tablet comprising an active drug.

25 It is yet still an additional objective of this invention to provide a tablet having one or more enhanced properties such as higher gloss, better mouthfeel, non-tackiness, being swallowable with little or no accompanying liquid, better taste and the like.

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The above objectives and other objectives are met in this invention which is more particularly described hereinafter without limitation.

BRIEF SUMMARY OF THE INVENTION

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In one embodiment, this invention comprises a tablet coating comprising gellan gum. In another embodiment, this invention further comprises a placebo or an active drug or pharmaceutical wherein the placebo or drug is coated with gellan gum. In another embodiment this invention further comprises a process for preparing a gellan gum composition useful for coating a placebo or a coated pharmaceutical tablet which comprises the steps of admixing gellan gum and water under effective shear conditions to prepare an aqueous gellan gum coating composition thereof. In another embodiment this invention further comprises preparing the aforementioned aqueous gellan gum coating composition and applying the same in an adherent fashion to a placebo or a tablet containing a pharmaceutical whereby a gellan gum coated placebo or gellan gum coated pharmaceutical tablet is formed and thereafter drying the same. In yet another embodiment of this invention, this invention comprises a method of treating a patient in need of treatment which comprises administering to the patient a therapeutically effective amount of a coated tablet, wherein said coated tablet comprises a tablet coated with gellan gum and which contains a therapeutically effective amount of a therapeutically effective drug beneficial to said patient. Other embodiments of this invention are included herein and are described in more detail hereinafter.

25

DETAILED DESCRIPTION OF THE INVENTION

Gellan gum useful herein is that produced by inoculating a carefully formulated fermentation medium with the microorganism *Sphingomonas elodea* (ATTC 31461). Gellan Gum is available from Monsanto Company, 800 North Lindbergh Boulevard, St. Louis, Missouri 63167, USA. Typical brand names include KELCOGEL®

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and GELRITE®. Gellan gum useful herein includes any form available form such as but not limited to, non-clarified, clarified, and partially-clarified native, deacetylated and partially deacetylated forms as well as mixtures thereof and the like. Kelcogel® and Gelrite® are registered trademarks of Monsanto Company. Gellan gum may be prepared according to the methods disclosed in U.S. Patent 4,326,052 and 4,385,123 both of which are incorporated herein their entirety by reference.

Optional components of the gellan gum aqueous coating composition of this invention may include but are not limited to a color additive(s) and/or other coating polymers as will be readily apparent to those of skill in the art in particular after reading this specification. A typical plasticizer is glycerine although any equivalent or substantially equivalent plasticizer may be satisfactorily employed herein if desired.

The scope and utility of the present invention is not limited to any active ingredient. Active ingredients which may be effectively coated using this invention are not limited and include illustratively pharmaceutical active ingredients and over-the-counter drugs (including vitamins and nutritional supplements and the like) such as those typically delivered in a tablet dosage form. Examples include but are not limited to analgesics and antiphlogistics such as aspirin, acetaminophen, phenacetin; steroids including antinflammatory steroids; enzymes, proteins, antibiotics or antimycrophotics including penicillin and its derivatives; anesthetics, vasodilators such as nitroglycerin, anticarcinogens, sulfonamide drugs, sedatives, tranquilizing and hypnotic agents, bronchial-dilating agents, potassium chloride, mixtures thereof and the like.

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The process for preparing a coated placebo or a coated (pharmaceutical) tablet comprising an active drug herein comprises the steps of admixing gellan gum and water under effective shear, heat and ionic conditions to prepare an aqueous gellan gum coating composition and applying the aqueous gellan gum coating composition in an effective fashion to a placebo or to a tablet such as one comprising a pharmaceutical whereby a gellan coated placebo or coated pharmaceutical tablet is formed. A drying step typically occurs and typically follows.

The aqueous gellan gum coating composition useful to coat tablets is preferably admixed in any suitable container or the like prior to applying the gellan gum composition to or on a tablet to be coated. Initially the gellan gum and water are admixed and further mixing is carried out under effective shear to form an aqueous tablet coating composition. Typically the gellan gum coating aqueous composition prior to application of such effective shear will have a viscosity in the range from about 44 cps. to about 55,500 cps. and preferably from about 2200 to about 50,000 cps although gellan gum compositions having greater and lesser viscosities may sometimes be employed depending on a number of factors.

If desired, gellan gum compositions comprising gellan gum and/or gellan gum and one or more of another ingredient such as a polymer such as, but not limited to, those selected from the group consisting of hydroxypropyl cellulose, hydroxypropyl methyl cellulose, sodium carboxymethyl cellulose, sugar, aspartame, maltodextrin, tapioca dextrin, modified food starches, polyvinylpyrrolidone, mixtures thereof and the like may be employed in this invention. As employed herein, the term "gellan gum" includes gellan gum and/or compositions of gellan gum with one or more of these polymers or a sugar.

The aqueous gellan gum composition of this invention may be mixed in or by any suitable mixing system preferably until substantially complete mixing has been

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accomplished. Some heating may be necessary to achieve dispersion and hydration of gellan gum. The amount of shear preferably employed is an effective amount, i.e., which produces a well mixed homogenous gellan gum composition. The aforementioned admixing can be carried out by any convenient means including but not limited to use of a propeller or stirrer system although generally stirring by a convenient mechanical means is acceptable. Other forms of mixing can be employed.

Optionally, if desired, various other ingredients may be employed in the gellan gum aqueous composition include any ingredient which is compatible or can be made compatible with an aqueous gellan gum composition useful to coat tablets of this invention, (such as, but not limited to, colors, color system(s), flavor(s), sweetener(s), mint(s), fragrance(s), plasticizer(s), active ingredient(s) and mixtures thereof and the like).

The gellan gum aqueous composition is preferably applied to the tablet(s) to be coated in a batch, semi-continuous or continuous process or some combination thereof in a manner which produces a satisfactorily uniformly coated tablet. The gellan gum composition may be applied to tablets to be coated using any satisfactory application and drying system or combination of some application system and some drying system. The combination is not critical nor is the arrangement of equipment.

The amount of gellan gum in the gellan gum aqueous composition useful for coating tablets is about 0.1% to about 10% and preferably from about 0 .25% to about 5% by weight gellan gum of the total gellan gum aqueous composition although greater and lesser amounts of gellan gum may be employed if desired. A most preferred range is about 0.075% to about 3 %.

During application of the gellan gum aqueous composition to the tablet to be coated, the temperature of the gellan gum aqueous composition is preferably in the

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range from about 25°C to about 45°C although greater or lesser temperatures may be employed if desired. It is preferred that the gellan gum composition be maintained in a solution or dispersion or an applicable state during its coating application to the tablet(s) to carry out this invention.

5

Historically those of skill in the art have considered a composition having a viscosity of about 1,000 centipoise (cps) as being at the upper bound as regards usefulness as a coating composition due to that high viscosity. Since an aqueous composition comprising gellan gum (1.8% by weight gellan gum) and water has a viscosity of about 28,460 cps at a temperature of about 30.°C, those of skill in the art would not have considered such a composition useful to coat tablets and would have been steered away from it for this invention. Now, however, the inventors have surprisingly discovered that despite the high viscosity of a gellan gum composition at room temperature that such compositions are very useful to coat tablets as the invention herein provides.

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Gellan gum may be coated onto tablets which are uncoated or are those tablets which have been coated with one or more prior coatings (overcoating) of an acceptable coating composition which allows adherency with gellan gum. An initial coating may comprise one or more polymers such as celluloses, dextrins, acrylics, any colors or other pharmaceutical coating material. A gellan gum composition may be employed as a primary coating on a tablet, as a secondary coating on a tablet, or as a tertiary coating if desired. One or more coating applications of gellan gum may be made to a coated or uncoated tablet in accordance with this invention, although typically one coating is effective and is preferred. If desired, a gellan gum coating may be applied to a tablet in accordance with the invention in an instance wherein a protective coating is desired, for example to protect coated or uncoated tablet from physical damage.

Typically the amount of gellan gum which is coated onto tablets in

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practicing this invention is that amount which provides a gellan gum coated tablet having a weight gain (during coating) from about 0.025% to about 10% weight percent of the total tablet weight and preferably from about 0.05% to about 5% weight percent of the total tablet weight although larger and smaller weight percents may be employed if desired. Typically this amount of gellan gum is that amount which is necessary to provide an effective or desired coating.

Neither the tablet shape nor the tablet size are critical. Preferred shapes and sizes are those which can be effectively consumed by a human or animal recipient with relative ease. Preferable sizes of tablets include but is not limited to those tablets which are about 1/4 inch to about $\frac{3}{4}$ inch in size and weigh from about 100 to about 1.5 grams each although tablets may be employed which are larger or smaller in size and of lighter and heavier weight if desired. Preferred shapes are round or oval; however, other shapes may be employed if desired.

15

Preferred tablets are medicinal tablets for humans or animals. The tablets include but are not limited to tablets of any convenient composition which may or may not contain any pharmaceutically effective drug vitamin or nutrient or drugs suitable for human and/or animal consumption. A gellan gum coating may be employed on tablets which are placebos or blanks. Tablets useful herein include but are not limited to tablets which are uncoated or have been coated one or more times. In one embodiment a gellan gum coating may be the only coating and may comprise a first coating or a second or a third coating.

25

Illustrative colors and colorants useful herein include without limitation, pigments, dyes, lakes and oxides (including titanium dioxide) and the like, may be optionally employed with gellan gum used in practicing this invention. The gellan gum aqueous composition may optionally contain a suitable color or colorants for application to a colored or noncolored coated or uncoated tablet.

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Tablets to be coated according to this invention may be colored, neutral or have their natural color or may be absent color. If one or more colors, dyes lakes, or pigments or mixtures thereof are employed in a gellan gum coating composition herein, such as for example, an FDA certified color, dye, lake, or pigment, the color or combination of colors is not critical and may be selected by those of skill in the art based upon a need at the time of the coating operation. Examples of suitable pigments which are useful in this invention include, without limitation, FD&C and D&C lakes, titanium dioxide, magnesium carbonate, talc, pyrogenic silica, iron oxides, channel black, insoluble dyes and mixtures thereof and the like. Also, nature pigments such as riboflavin, carmine 40, curcumin, annatto, mixtures thereof and the like are acceptable herein. Other examples of pigments suitable herein include, without limitation, these disclosed in Jeffries U.S. Patent No. 3,149,040 and Butler et al., U.S. Patent 3,297,535, as well as in Colorcon U.S. Patent No. 3,981,984. These three patents are incorporated herein by reference in their entirety. In the absence of a colorant, the gellan gum composition typically produces a clear or substantially clear coating on a coated tablet.

As employed herein, the term "tablet" includes without limitation, tablet, particle, micronized particle, particulate, pellet, pill, core, powder, granule, granulate, small mass, seed, specks, spheres, crystals, beads, agglomerates, mixtures thereof and the like. Typically the preferred tablet will be in a form sufficiently stable physically and chemically to be effectively coated in a system which involves some movement of the tablet, as for example in a fluidized bed, such as in a fluidized bed dryer or a side vented coating pan, combinations thereof and the like. Virtually any tablet, placebo, the latter typically lactose or sugar or mixtures thereof and the like, is acceptable herein as a tablet to be coated in the practice of this invention.

Tablets coated according to this invention have a high gloss. Typically the gloss is in the range from about 200 to about 400 and preferably from about 250 to about 350 although greater or lesser gloss may be employed if desired. As referred to above,

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gloss is measured or characterized typically by use of a Tricor Systems, Inc., Model 805A, Surface Analysis System. Tablets of this invention typically have one or more enhanced properties such as higher gloss, better mouthfeel, non-tackiness, being swallowable with little or no accompanying liquid, better taste and the like.

5

The gloss resulting from gellan gum coating of this invention is superior in shine to conventional film coatings presently used in the industry. Measurements of gloss on polymer coated tablets and commercial products were well below the gloss imparted with gellan gum prepared in accordance with this invention as measured at TRICOR Systems. Gellan gum coatings of this invention impart this gloss at weight gain levels that are considerably lower than existing and accepted alternatives. As a result of this high gloss from comparatively lower weight gains brought about by this invention, gellan gum is an attractive alternative to existing aqueous form coatings.

15

This characteristic high gloss from low weight gains also makes gellan gum an attractive alternative to sugar coating processing currently used in the industry. Sugar coating processes currently use multiple materials, extended processing times and multiple material handling steps. Superior gloss can be achieved with gellan gum at a fraction of the weight gain now required in sugar coating. This lower material requirements results in glossy tablets that can be manufactured much faster than current products and can also be formulated to produce a smaller, easier to swallow dosage.

20

As employed herein, the term "adherent" means that the gellan gum coating effectively adheres to the coated tablet until consumption by a patient or animal to enable effective release of the active ingredient therefrom so that the active is effectively made available to the patient's biological systems to provide therapeutic value.

25

Although the gellan gum coating composition of this invention will initially be an aqueous composition, the tablet coating will preferably be dried or

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substantially dried prior to, upon its exit or removal from the coating application system or at sometime in preparing coated tablets. The coated tablets may be placed in suitable packaging then if desired.

5 The amount of coating provided to the surface of the tablet is an effective amount and is typically that amount which provides a minimum effective coverage of the exterior surface area of the tablet, although this invention also encompasses those instances where there is partial coverage of the exterior surface as well.

10 If desired, one or more layers of gellan gum coating may be employed using this invention. Those of skill in the art will be able to determine the extent of any layering depending on the drug, tablet size, and its physical and chemical and therapeutic properties and characteristics from a reading of this specification and using their skill in the art.

15 It is preferred that coating be continuous or nearly continuous and over the surface of the tablet. An effective depth of coating is provided for retention. It is also desired that the tablet coatings herein be somewhat resilient with respect to handling, to peeling and to flaking and being rubbed off the coated tablet.

20 As referred to above, application of the gellan gum aqueous composition as a coating to the tablet is preferably carried out by placing a tablet capable of receiving and adhering a gellan gum tablet coating composition of this invention in any acceptable coating application system. An acceptable coating application system is illustratively any system which has the capability to apply a gellan gum coating composition of this invention to a tablet to provide an effectively, preferably uniformly coated tablet. For example, an acceptable coating application system includes without limitation, a plain fluid bed system (i.e., one without any "Wurster" type insert), including a fluid bed spray

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tower of any reasonable size and design and systems similar thereto in function and utility.

Air Suspension Coating systems useful here as an illustrative application
5 system include those described in Ullman's Encyclopedia of Industrial Chemicals,
Volume A16 pages 583-584 (1990) which includes a description of the Wurster process.
Ullman's Encyclopedia of Industrial Chemicals, Volume A16 pages 583-584 (1990-1996)
is incorporated herein by reference in its entirety. This incorporation includes the chapter
Microencapsulation authored by Christopher A. Finch of Pentafin Associates, Weston
10 Turville, AYLESBURY HP 22 5TT, UK.

Also, acceptable for use to prepare coated tablets of this invention are
illustratively a variety of side vented coating pans, spray dryer(s), continuous coating
pans, and conventional coating pans, such as those with systems for mechanically
15 providing the gellan gum composition to a tablet in an effective manner using mechanical
means as for example by spray nozzles or the like. Also acceptable as a spray tower
system is a conventional fluid bed tower equipped with a suitable spray apparatus. Any
application system capable of applying a composition of this invention to a tablet is an
acceptable system for coating tablets employing the aqueous gellan gum coating
20 composition of this invention. As the coating system is not critical, any size coating
system is acceptable. Batch and continuous processes, semi-continuous and suitable
variations thereof are envisioned without limitation.

The "Wurster" type fluid bed dryer typically comprises a cylindrical outer
25 vessel having a perforated floor through which a heated gas passes upwardly to heat and
fluidize a batch of tablets or particles fed to or formal therein. A concentric, open ended
inner cylinder is suspended above the center of the perforated floor of the outer vessel. A
spray nozzle, or projecting part, centered beneath the inner cylinder sprays a solution of
the coating material upwardly into the inner cylinder as the fluidized materials pass

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upwardly through the spray in the inner cylinder. The particles circulate upwardly though the center of the inner cylinder and downwardly between the inner and outer cylinder. The air that fluidizes the particles also serves to vaporize the water causing the composition to deposit as a film or coating onto the surface of each particle. After 5 repeated passes through the coating zone in the inner cylinder, a sufficient thickness of polymer accumulates over the entire surface of each particle as to coat each particle. A description of an acceptable "Wurster" type fluid bed dryer is found in J. Am Phar. Assoc, Sci. Ed. Vol 48, (1959) Air Suspension Technique of Coating Drug Particles by Wurster, Dale E. and Preparation of Compressed Tablet Granulations by the Air 10 Suspension Technique II, Wurster, Dale E, Sci Ed Vol 49 (1960) both of which are incorporated herein in their entirety by reference. In operation of the dryer, the operator will typically have the tablets discharged when the desired amount of coating has been applied to the tablets. This is generally based on the amount of coating composition sprayed in the dryer from which based on prior experience, the amount of weight gain 15 (%) of the tablets during coating can be determined. Electronic or equivalent controls are typically installed on the dryer to regulate the process such as regulating the temperature of the inlet air and the amount of such inlet air and its pressure.

In side vented coating pan systems, as the material inside is coated it 20 increases in size and weight. Generally the materials to be coated accumulate adjacent an end wall and along a side wall of the drum in the system. As the drum rotates, the material is tumbled and is coated with a coating composition from one or more spray nozzles. Initially the material may form a mass and as the material is sprayed and increased in size the large particles migrate away from the end wall and cannot penetrate 25 the mass of smaller particle adjacent the end wall. Eventually, substantially all of the material is uniformly coated a such that the material forms a new mass wherein the particles are slightly larger than the original mass formed by the uncoated particles. The process repeats itself such that the particles are coated with additional composition from

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the spray nozzle, thereby again increasing in size and weight and migrating away from the end wall. The cycle continues until the particle achieve a desired uniform size.

Particularly useful self contained side vented coating pan system in this
5 invention are available under the Accela Cota brand sold by Thomas Engineering
Incorporated, 575 West Central Road, Hoffman Estates, Illinois, 60195-0198, U.S.A.
Various size pans may be satisfactorily employed herein and include without limitation
15, 24, 48 and 60 inch pans, if desired. The size of the pan and dryer are not critical. The
Compu Lab model sold under the Accela Cota brand works well for laboratory size
10 charge (feed) quantities. Those of skill in the art will recognize that various size pans
may be employed depending on the amount of materials to be coated and other coating
operations.

The Accela Cota brand side vented coating pan system comprises a
15 rotating drum and as the drum is rotated containing the tablets to be coated, the coating
composition is applied to the tablets by means of one or more nozzles positioned within
the rotating drum so as to direct the coating composition to the tablets in the bed. As the
pan is rotated and the coating composition is further applied to the tablets, the tablets
achieve a desired coating. This apparatus is also a dryer for substantially drying the
20 tablets as the tablets are coated. The side wall of the drum is perforated and a flow of air
is provided into the drum through apertures for drying the coating composition on the
tablets. A system is also provided on the apparatus for removing the outlet air and for
removing the coated tablets.

25 The nozzles of this side vented coating system are preferably adjustable
and may be positioned nearer to and closer to the bed of tablets to be coated depending on
the conditions of use and the desired coating composition quality and quantity, among
other factors. Those of skill in the art will recognize that the distance of the nozzle or
nozzles from the bed is important and may be adjusted to provide optimum coating

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compositions. In operation such nozzle placement distances will be an effective distance and will be selected from a plurality of available positions and will depend on the tablets being coated, the coating compositions, the degree of coating desired and other conditions of the particular coating operation, among other factors.

5

Those of skill in the art will recognize that one or more nozzles may be employed as desired to provide optimum coating. The number of nozzles is not critical and may be varied as needed depending on the coating operation and other factors. The nozzle throat diameter is typically from about 0.028 inch to about 0.100 inch although, 10 greater and smaller throat diameters may be employed. A nozzle throat diameter of somewhere about 0.040 inch is preferred although that size is not critical. The nozzle(s) is preferably aimed perpendicularly or nearly perpendicular to the bed although other direction(s) of aim may be employed if desired. Those of skill in the art will recognize that the pan may be rotated at a speed selected from a plurality of operating speeds. The 15 pan may be stopped after the material has been coated and the matter removed.

20

In general, an effective nozzle distance for applying a coating to a tablet using a side vented pan coating system is in the range from being positioned less than about a 1/4 inch from the bed to about 15 inches and preferably from about 8 to about 12 inches although greater or lesser nozzle distances may be employed if desired depending on the weight of tablets charged into the pan and coating system composition and other factors.

25

If desired, the same or a similar coating application system can be employed for both a first and a second or sequential coating applications or different coating application systems may be employed for a first or second or more coating applications. If desired, the same coating application system can be used to apply a first and second or more coatings with or without removal of the tablets from such a system between the first and second or more coatings.

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While illustrative useful application systems have been described herein, those of skill in the art will recognize that such description is provided to provide information as to the possible application and use herein in accordance with this invention. Those of skill in the art will recognize that the actual operation of any such application system will vary and may be varied from "text book" type description of such operation in according with the parameters and conditions of any desired operation, among other factors. Configurational and design changes may be made on such applications systems and operating parameters may be varied.

10 The gellan gum coated tablets of this invention may be internally consumed by humans and animals in a typical customary manner.

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EXAMPLES

Examples 1-18, are provided to illustrate the preparation of acceptable coated tablets in accordance with this invention and are provided by way of illustration and are not intended to limit the invention in any way. All percents and any parts are by weight unless otherwise indicated. These Examples illustrates the practice of this invention in a non limiting fashion. Various application systems including fluidized feed systems and pan vented coated systems are illustrated without limitation.

10 EXAMPLE 1

An acceptable high gloss gellan gum coated (red colored) tablet was prepared in this Example in accordance with this invention.

15 A gellan gum composition useful for coating tablets was prepared comprising 30 grams gellan gum, 1968 grams water and two grams sodium citrate to provide a 1.5% by weight gellan gum aqueous composition useful for coating tablets.

20 This aqueous gellan gum composition was prepared by weighing the water into a clean dry residue free beaker and weighing out the gellan gum (Kelcogel) and sodium citrate. The water was then mixed with a laboratory mixer to create a vortex. The gellan gum powder and sodium citrate was slowly introduced into the vortex to achieve dispersion. Stirring was continued without heat to finalize the dispersion of gellan gum. Heat was applied while stirring until the dispersion temperature was about 25 70°C to hydrate the gellan gum. Care was taken to avoid charring the resulting dispersion, i.e. employing sufficient stirring and avoiding overheating. The beaker was removed from the stir plate and cooled to ambient temperature to make the gellan gum aqueous composition available for coating.

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The tablets to be coated herein were uncoated placebos (1/2 inch, standard concave shape, 390 mg. weight each).

A hydroxypropylmethylcellulose (HPMC) and color composition having 5 the ingredients shown in Table 1 below was applied to these uncoated placebos to prepare a tablet which had color and appearance mimicking recognized commercial products using a Compu Lab side vented 15 inch coating pan system as an application system.

TABLE 1

	Ingredients:	Weight (g)
10	Pharmacoat 606 (10%)	1800
	D-447	90
	TA	30
15	Water	<u>130</u>
	Total Weight	2050 grams

	Red (D447) (Dye Dispersion)	
20	11.83% Titanium Dioxide	23.64 grams
	20.01% FD&C Red No. 40, Hi Dye Lake	40 grams
	8.18% FD&C Yellow No. 6 dye	16.36 grams
	2.0% EDTA solution (40%)	4 grams
	57.98% Distilled Water	<u>115.91</u> grams
		199.91 grams

25
Pharmacoat 606 (10%) = hydroxypropyl methyl cellulose
TA = triacetin (plasticizer)

30 The side vented pan coating system used herein employed one nozzle which was aimed more or less directly at the bed of tablets to be coated and was positioned at a acceptable standard distance from the outer portion of that bed. That nozzle had a throat diameter of about 0.040 inch. Operating data was:

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TABLE 2

Side Vented Coating Pan Operating Data, 1.9 Kg. Charged						
		Temperature, °F				
Elapsed Time (Min)	Coating Composition Wt(g) Sprayed	Inlet	Outlet	PAN RPM	Pan Air Flow (CFM)	Atomizing Air (PSI)
0	0	72.0	49.0	10.2	238	45.2
4:10	38	69.5	48.5	10.2	238	44.6
10	117	68.5	49.4	10.2	238	44.3
15	190	64.2	48.8	10.3	238	44.4
20	261	65.1	49.0	10.3	238	44.1
25	233	60.8	47.7	10.3	238	44.2
30	406	62.1	47.8	10.3	238	44.0
34:05	466	61.9	47.8	10.3	238	44.1

15

These placebos (red colored) were then coated with the gellan gum aqueous composition (prepared in a first step of this Example) in the same 15 inch diameter pan Compu Lab side vented coating system as an application system, the data of which is shown in the following Table 3.

20

25

30

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TABLE 3						
Side Vented Coating Pan Operating Data						
Charge = 1.9 Kg. plus color coating						
		Temperature, °F				
Elapsed Time (Min)	Solution Wt(g) Sprayed	Inlet	Outlet	PAN RPM	Pan Air Flow (CFM)	Atomizing Air (PSI)
5	0	64.5	46.6	24.3	200	25.9
10	4	73	61.2	24.3	220	25.4
15	8	126	66.3	24.3	220	25.5
20	12	178	64.8	24.3	220	25.3
25	16	225	65.1	24.3	220	25.2
30	20	271	62.3	24.3	220	25.4
35	24	318	63.1	24.3	220	25.2
40	28	365	61.0	24.3	220	25.1
45	32	407	59.0	24.3	220	25.6
50	36	453	60.3	24.3	220	25.5
55	40	499	60.0	24.3	220	25.1
60	44	544	59.9	24.3	220	25.5
65	48	589	60.1	25.0	220	25.3
70	52	634	60.0	25.0	220	25.1
75	56	678	59.9	25.0	220	25.5
80	60:30	730	60.0	25.0	220	25.3
85	64:30	775	60.6	25.0	220	25.0
90	67:20	807	59.9	25.0	220	25.0

This application system employed one nozzle positioned in close proximity to the tablet bed and aimed at the bed of tablets to be coated. This produced an acceptable high gloss gellan gum coated placebo.

30

Samples were taken after weight gains of 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 0.7% respectively to document and monitor coating appearance and character. Further, this Example provided acceptable tablets with very high gloss and lubricious mouthfeel. This Example demonstrates the gloss and mouthfeel attributes of the gellan gum coating of this invention and also demonstrates the compatibility of clear gellan gum

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coating with a base coating of polymer and lake color system. Tablets of this Example had a gloss equal to or better than the gloss of commercially available sugar coated products.

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EXAMPLE 2

In a first step, an acceptable gellan gum aqueous coating composition was prepared according to Example 1.

5

The tablets to be coated herein comprised uncoated placebos (3/8 inch, rounded shape, 355 mg. weigh each, standard concave shape). These uncoated placebos were first coated with a polymer/color composition comprising:

10

Table 4

	Ingredients:	Weight (g)
15	606 (10%)	2000
	SS-1092	125
	TA	33
	Water	<u>200</u>
	Total Weight	2358g

20	Brown (SS-1092) (40% solids):	
	37.2% Titanium Dioxide	37.2 grams
	2.65% FD&C Yellow No. 6 Low dye Lake	2.65 grams
	0.15% Red Iron Oxide	0.15 grams
	2.0% EDTA solution (40%)	2.00 grams
	58.0% Distilled Water	<u>58.00 grams</u>
		100.00 grams

25 SS = Spectrablends, from Warner-Jenkinson*

*Warner-Jenkinson: 107 Wade Avenue, South Plainfield, New Jersey 07080

30 This coating operation was carried out in a Compu Lab 15 inch side vented coating system in a manner similar to that employed for the color coating in Example 1, above.

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These once coated placebos were then fed to a Compu Lab 15" pan side vented coating system wherein a gellan gum coated high gloss tablet was prepared. One nozzle was employed which was positioned in close proximity to the bed of tablets to be coated.

5

Operating data is provided in Table 5 below.

10

TABLE 5 Side Vented Coating Pan Operating Data						
		Temperature, °F				Atomizing Air
Elapsed Time (Min)	Solution Wt(g) Sprayed	Inlet	Outlet	PAN RPM	CFM	PSI
0	0	68.1	49.2	24.2	255	20.1
5:15	88	68.6	48.3	24.2	255	19.7
10:15	191	70.0	48.5	24.2	255	19.9
15	295	70.0	48.8	24.2	255	19.5
20:30	421	70.1	49.0	24.2	255	19.5
25	524	69.9	49.0	24.2	255	19.7
30	643	70.4	49.3	24.2	255	19.9
35	762	70.2	49.8	24.2	255	19.2

15
20
25

Samples were taken after weight gains of 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6% respectively to monitor coating character. This Example provided acceptable tablets of this invention with high gloss and lubricious mouthfeel. This Example demonstrates the compatibility of clear gellan gum coating with polymer/oxide color systems in the base coat.

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EXAMPLE 3

High gloss gellan gum coated tablets were prepared by preparing in a first step a gellan gum composition as described in Example 1 above which contained 1.5%
5 Kelcogel and 0.15% aspartame.

The tablets to be coated herein comprised uncoated placebos which were
coated with a polymer/color composition comprising:

10

Table 6

15

Ingredients:	Weight (g)
606 (10%)	600
D452 (40%)	24
PEG460	12
Water	<u>42</u>
Total Weight	678

20

Red (D452) (Dye Dispersion)	
12.0% Titanium Dioxide	420 grams
20.0% FD&C Blue 1, Hi Dye Lake	700 grams
2.00% FD&C Yellow No. 6 dye	70 grams
6.0% FD&C Red No. 40 dye	210 grams
2.5% EDTA solution (40%)	87.5 grams
57.5% Distilled Water	<u>2012.5 grams</u>
	3500 grams

25

The application was carried out in a Compu Lab side vented coating 15"
pan, the data of which is shown in Step A below.

30

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TABLE 7						
Step A Side Vented Coating Pan Operating Data						
		Temperature, °F				Atomizing Air
Elapsed Time (Min)	Solution Wt(g) Sprayed	Inlet	Outlet	PAN RPM	CFM	PSI
0	0	69.9	47.4	15.0	245	42.1
6	95	70.2	45.5	15.0	250	41.4
8	137	70.2	46.6	15.0	250	41.3
12	213	69.9	46.9	14.9	250	41.4
17:10	305	67.3	46.5	15.0	235	39.9
18	323	67.6	46.3	14.9	235	39.7
20	362	68.0	46.6	14.8	235	39.6
24:10	493			15.1		

15

The once coated placebo from Step A above was then coated with a gellan gum aqueous composition in a Compu Lab side vented coating 15" pan in a Step B

TABLE 8						
Step B						
		Temperature, °F				Atomizing Air
Elapsed Time (Min)	Solution Wt(g) Sprayed	Inlet	Outlet	PAN RPM	CFM	PSI
0	0	75.5	50.6	24.4	255	24.4
4	69	69.1	47.3	24.4	270	24.4
8	144	72.3	50.0	24.4	255	24.4
12	237	67.2	49.7	24.4	270	24.3
16	321	72.6	49.1	24.4	260	24.1
20	413	72.1	49.8	24.4	260	24.4
24:30	519	72.1	49.6	24.4	260	23.4
28:30	612	72.1	50.4	24.4	255	23.8

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A sweet tasting high gloss acceptable coating was produced.

Samples were taken after weight gains of 0.1, 0.2, 0.3, 0.4 and 0.5% respectively to monitor coating character. Acceptable tablets were prepared in this
5 Example which had high gloss and lubricious mouthfeel. This demonstrates the compatibility of clear gellan gum coating with polymer/dye color systems in the base coat.

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EXAMPLE 4

An acceptable tablet coating composition comprising a gellan gum composition was first prepared according to Example 1.

5

The tablets to be coated herein comprised uncoated active drug ingredient tablets of about 400 milligram (mg.) weight each, which were first coated with a polymer/color coating composition comprising:

10

TABLE 9

	Ingredients:	Weight (g)
	Pharmacoat 606 (10%)	100
	D-947	4
	TA	2
15	Water	<u>42</u>
	Total Weight	148
20	Pink (D947) (Dye Dispersion)	
	37.6% Titanium Dioxide	47 grams
	2.4% D&C Red No. 27 dye	3 grams
	1.6% EDTA solution (40%)	2 grams
	58.4% Distilled Water	<u>73 grams</u>
		125 grams

25

TA=triacitin

A fluidized bed dryer system ("Wurster" type) was employed to carry out a first coating of these initially uncoated tablets. The fluidized bed system comprised a 4 inch circular plexiglass column having a perforated base plate with about 150 holes each about 1/8" diameter therein and having positioned in this base plate, a liquid spray nozzle which protruded about 1/4 inch in the interior of the column above the base plate. The spray nozzle had a 0.035 inch diameter throat and was connected externally to a coating solution supply system. An air supply system was connected to the base plate and an air outlet filter positioned atop the column provided for the air outlet. The air supply system had a temperature regulator system on it. In operation the tablets to be coated were

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charged to this fluid bed dryer, compressed air was forced into and through the base plate and color coating composition was sprayed by the spray nozzle into the bed of tablets from the coating solution supply system.

TABLE 10

Elapsed Time (Min)	Solution Wt(g) Sprayed	Feed	Outlet Temp°F	Blower	Compressor PSI
0	11.3	2.2	120	5	32
4	65	2.2	120	5	36
8	20	2.2	116	5.5	36

An acceptable high gloss tablet was then prepared by coating over the color coated tablets prepared immediately above in the same fluidized bed dryer as described above by applying the previously made gellan gum coating composition of this Example to the color coated tablets. In this coated active product tablet, the color coat was the first coating (primary, initial, or base) and gellan gum was the second coating or overcoating.

TABLE 11

Elapsed Time (Min)	Solution Wt(g) Sprayed	Feed	Outlet Temp°F	Blower	Compressor PSI
0	0	2.5	120	5	32
4	46	2.5	120	5	32
8:10	92	2.5	122	5	32
12	134	2.6	122	5	32
16	179	2.6	122	5	32

Tablets produced in this Example were acceptable and had high gloss and lubricious mouthfeel. These tablets were essentially the same as the acceptable tablets produced in the previous Example. In this Example, a fluid bed system was employed as an

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application system whereas a side vented coating pan was employed as an application system in the previous Example.

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EXAMPLE 5

An acceptable gellan gum coating composition was prepared according to
Example 1.

5

The tablets to be coated herein comprised active ingredient tablets of about 476 mg weight each, which was first coated with a polymer/color coating composition comprising:

10

TABLE 12

15

Ingredient	Weight
606 (10%)	100.0
D-452 (40%)	4.0
PEG 400	2.0
Water	<u>7.0</u>
Total Weight	113.0 g

20

Red (D452) (Dye Dispersion)	
12.0% Titanium Dioxide	420 grams
20.0% FD&C Blue 1, Hi Dye Lake	700 grams
2.00% FD&C Yellow No. 6 dye	70 grams
6.0% FD&C Red No. 40 dye	210 grams
2.5% EDTA solution (40%)	87.5 grams
57.5% Distilled Water	<u>2012.5 grams</u>
	3500 grams

25

This first coating was carried out in a fluidized bed dryer as described in Example 4.

30

35

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TABLE 13

			Temperature, °F			
Elapsed Time (Min)	Solution Wt(g) Sprayed	Feed	Inlet	Outlet	Blower	Compressor PSI
5	0	2.2	186	132	5	32
	4	47	186	127	5	32
	8	87	186	127	5	32
	10:30	108	187	129	5	32

10 In a second step of this Example 5, a high gloss gellan gum coated tablet was prepared by coating the once coated tablet prepared immediately above in a fluidized bed dryer as described above with a gellan gum composition, the data of which follows in
15 Table 14.

TABLE 14

			Temperature, °F			
Elapsed Time (Min)	Solution Wt(g) Sprayed	Feed	Inlet	Outlet	Blower	Compressor PSI
20	5	53	2.35	179	127	5
	9	89	2.4	179	128	5
	14	137	2.4	178	127	5
	21:30	200	2.4	176	125	5

25 30 Tablets produced in this Example were acceptable and had high gloss and lubricious mouthfeel. These tablets were essentially the same as the acceptable tablets produced in the previous Example.

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EXAMPLE 6 - Application of a Clear Gellan Gum Coating to an Uncoated Tablet

Purpose: To apply clear coating of an aqueous gellan gum composition to uncoated uncolored tablets to provide an acceptable high gloss coated tablet of this invention.

5

Method: Using a 1.5% gellan gum solution useful for coating tablets

	%	Grams
10	1.5 % Gellan Gum	22.5 grams
	0.10% Sodium Citrate**	1.5 grams
	98.4% Deionized Water	<u>1476.0 grams</u> 1500 grams

15 ** Dihydrate, powder

Using a suitable mixing blade and mixer, with good vortex the gellan gum was slowly added to water. Once the gellan gum was dispersed sodium citrate was added and heating initiated. Heat to 70°C. Allow solution to cool and form gel.

20

Coating procedure: Spray 200 grams of 1.5% gellan solution (room temperature) onto 420 grams uncolored active ingredient tablets using a laboratory fluidized column (similar in concept to an Aeromatic Strea 1). Samples of tablets were taken at 0.05, 0.1, 0.2, 0.3, 0.4 and 0.5% weight gains respectfully.

25

30

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Application of 1.5% Gellan Gum to Uncoated Tablet

	Time Min.	Weight Sprayed Grams	Inlet Temp (°F)	Exhaust Temp (°F)	Pump Setting	Compressor PSI
5	0	5.5	162	127	2.5	32
	4:30	58.5	168	119	2.5	30
	8:30	100.0	173	123	2.5	32
	13:00	146.5	173	123	2.5	32
	16:00	177.5	175	123	2.5	32
	18:40	200	175	123	2.5	32

In this Example, acceptable tablets were produced which had very high gloss and lubricious mouthfeel. This Example demonstrates that gellan gum coating of this invention can be successfully coated onto a tablet absent a base coating on that tablet.

The resulting gloss was judged superior to commercially available clear coatings (non gellan gum) and commercially available sugar coatings.

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EXAMPLE 7 - Preparation and evaluation of the viscosity of 1.8% and 2.0% gellan gum composition to be measured for viscosity over a temperature range of about room temperature to about 60°C and also to be coated onto color coated tablets.

These solutions of gellan gum were sprayed onto color coated tablets at temperatures between 24°C and 30°C (with viscosities ranging from +28,000 cps to 55,000 cps).

Materials: Gellan Gum
10 Deionized Water
Na Citrate

Procedure: A 1.8% gellan and a 2% gellan solution were made as Example 1

1.8%

15	Gellan Gum =	1.8% =	27.9g
	Deionized Water =	98.08% =	1471.2g
	Na Citrate =	0.12% =	<u>1.8g</u>
		TOTAL	1500g

2.0%

20	Gellan Gum =	2.0% =	30.0g
	Deionized Water=	97.87% =	1468.05g
	Na Citrate =	0.13% =	<u>1.95g</u>
		TOTAL	1500g

25

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Viscosity Measurements:

Spindle=3, Vessel=600 ml beaker, DV-I+ Brookfield Viscometer, Viscosity was measured while solutions cooled.

5	1.8% by wt. Gellan Gum			2.0% by wt. Gellan Gum		
	Temp. °C	Viscosity (cp)	Speed RPM	Temp °C	Viscosity (cp)	Speed RPM
	-	-	-	--	--	--
60	44	100	--	--	--	--
50	60	100	48	89	100	
40	127	100	40	164	100	
35	2200	50	34.6	17680	5	
*30	28460	2.5	30	39740	2.5	
**25	38730	2.5	*28	45600	2.0	
--	--	--	**24.6	55440	2.0	

Key:

*Viscosity measured before start of coating application to tablets

**Viscosity measured after coating application was completed to tablets

20

25

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1.8% Gellan gum

Brookfield Engineering Laboratories, Inc., 240 Cushing Street, Stoughton, Massachusetts
02072-2398

5 Application as a Coating to a Tablet Using a Fluid Bed Dryer

	Time Min.	Weight Sprayed	Inlet Temp°F	Exhaust Temp°F	Pump Setting	Compressor PSI	H/B
10	0	5.5	158	131	2.5	32	H8
	4:00	54.0	103	121	2.5	30	B5
	8:00	92.0	167	122	2.5	32	B5
	12:30	137.5	168	122	2.5	31	B5
	16:30	176.5	167	123	2.5	32	B5
	20:00	200	169	123	2.5	32	B5

15

The temperature of 1.8% Gellan at end of run was 26.0°C.

2% Gellan Gum

Application as a Coating to a Tablet Using a Fluid Bed Dryer

	Time Min.	Weight Sprayed	Inlet Temp°F	Exhaust Temp°F	Pump Setting	Compressor PSI	H/B
20	0	6.0	174	140	3.0	32	H8
	1:00	22.0	170	128	3.0	32	
	4:00	72.0	174	119	2.5	32	
	8:00	113.0	177	127	2.5	32	H8
	14:00	180.0	176	127	2.5	32	B5.6
	15:45	200	178	128	2.5	32	

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There was no problem spraying an aqueous gellan gum composition at 1.8% or 2.0% at room temperature at a viscosity ranges between about 28,460 cps at about 55,500 cps using conventional peristaltic pumping and standard nozzle apparatus.

5 Samples were taken after weight gains of 0.05, 0.1, 0.2, 0.3, 0.4 and 0.5% respectively to monitor coating character. In this Example, acceptable tablets were produced having high gloss and lubricious mouthfeel. This Example showed that gellan gum aqueous coating compositions can be successfully employed according to this invention at 1.5%, 1.8% and 2.0% solids. Gloss and mouthfeel are not compromised
10 when applying (via spraying) higher solids coating compositions.

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EXAMPLE 8 - Preparation of a 1.8% by weight and 2.0% by weight aqueous gellan solution to be used for spraying a clear coating of gellan gum onto a color coated tablet.
The gellan gum solutions will be sprayed at an elevated temperature.

5 Materials: Gellan Gum
Deionized Water
Na Citrate

Procedure: **Solutions were made:**

<u>1.8% Gellan Solution (1L) Prepared</u>		
Gellan Gum =	1.8% =	18.0g
Deionized Water=	98.08% =	980.8g
Na Citrate =	0.12% =	1.2g
	TOTAL	1000g

<u>2.0% Gellan Solution (2L) Prepared</u>			
Gellan Gum =	2.0% =	40g	
Deionized Water=	97.87% =	1957.4g	
Na Citrate =	0.13% =	2.6g	
	TOTAL	2000g	

Prepared gellan solutions (1.8% concentration and 2.0% concentration) were then sprayed onto tablets using the fluid bed coating equipment. The solution were sprayed at 40°C where viscosity of each solution is below 200 cps.

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1.8% Gellan Gum Solution at 40°C

	Time	Weight Sprayed	Inlet Temp°F	Exhaust Temp°F	Pump Setting	Compressor PSI
5	0	0	142	125	2.3	32
	4:00	32	159	127	2.3	32
	8:30	75.5	172	125	2.3	32
	12:00	109.5	169	126	2.3	32
	18:25	166.6	164	125	2.3	32

10 2.0% Gellan Gum Solution at 40°C

	Time	Weight Sprayed	Inlet Temp°F	Exhaust Temp°F	Pump Setting	Compressor PSI
15	0	0	150	127	2.3	32
	8:00	75.5	168	127	2.3	32
	14:00	174.5	166	127	2.3	32
	16:42	150	165	128	2.3	32

Heating the solution to lower viscosity had no detrimental effect on the coating delivered to the tablets. Spraying at elevated temperatures allows for high solids at lower viscosity and delivers a film comparable to lower solid solutions sprayed at room temperature.

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EXAMPLE 9 - Gellan with pigment sprayed onto tablets. Pigment addition to gellan coating solutions at room temperature is difficult due to viscosity of gellan solution. Pigment is easily dispersed, however, when gellan coating solution is heated to 40°C or above. At this temperature the coating solution is fluid (viscosity below 200 cps) and dispersion of pigments in gellan solution is easily achieved with a standard laboratory mixer.

5

Gellan solution: Follow procedure recited in Example 1.

Formula:

1.5% Gellan gum	45 grams
10 0.1% Sodium Citrate	3 grams
98.4% Deionized Water	2952 grams

10

Sodium Citrate (a sequestrant)

15

1000 grams of above gellan coating solution (1.5% gellan) is held at 40°C. To this preparation is added 3.0 grams Propylene Glycol and 3.0 grams of Lecithin (Alcolec F-100) while mixing. The color component (7.5 grams of Green - Spectra Spray SS-1091) is added but while mixing and holding solution temperature at 40°C or above. Mix until homogenous.

15

Grams of gellan/color preparation from above was then sprayed onto 420 grams of tablets in a fluidized bed coating apparatus. The 420 grams of tablets is a combination of 25 grams of tablets with active ingredients and 395 grams of placebo tablets. Samples of tablets were taken at 0.5, 1.0, 2.0, 2.5 and 3.0% weight gains respectively.

20

Tablets prepared in this Example had high gloss, uniform color and lubricious mouthfeel. This Example demonstrates the compatibility of gellan gum with lake color system for aqueous film coating.

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EXAMPLE 10 - Gellan clear coating sprayed on gellan/color coated tablets from
Example 9

Tablets from Example 10 which were coated with gellan and color coating
5 solution (gellan, Green Spectra Spray, Propylene Glycol and Lecithin) were taken and
coated again with a clear gellan coating solution also sprayed at 40°C (1.5% gellan). This
demonstrates the compatibility of gellan/color coating with gellan when used as a top
coating or gloss coat. The top coating of clear gellan was applied at 40°C with a total
10 weight gain of 0.5%. Samples were taken at 0.05%, 0.1%, 0.2%, 0.3%, 0.4% and 0.5%
with gloss increasing with each additional weight gain of clear coating.

Tablets prepared in this Example had a higher gloss than the tablets of Example 10.
These tablets also had a lubricious mouthfeel. This Example demonstrates the ability of
15 this invention to improve tablet gloss when using clear gellan gum coating as an overcoat
or as a gloss coating. This Example also demonstrates the compatibility of gellan gum
coating with a base coat comprising gellan gum and lake color. Coated tablets produced
herein have gloss and appearance which is better than or equivalent to commercially
manufactured sugar coated tablets.

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EXAMPLE 11 - Gellan gum with pigment (oxides)

Using 1.5% gellan gum solution prepared in example 11, maintain gellan solution at 40°C and add color/plasticizer system as in example 10.

5

Color system added to 1000 gram gellan solution:

3.0 grams Lecithin (Alcolec F-100)

3.0 grams propylene glycol

7.5 grams Oxide (Spectra Spray 1092)

10

Pigment disperses easily in gellan solution at 40°C because of low viscosity of heated solution.

15

760.1 grams of gellan/oxide preparation were sprayed at 40°C onto 420 grams of tablets in a fluidized columns (similar to Aeromatic Strea 1). Samples were taken at 0.05%, 0.1%, 0.2%, 0.3%, 0.4% and 0.5% weight gains.

20

Tablets were produced in this Example that had high gloss, uniform color and lubricious mouthfeel. This Example demonstrates the compatibility of gellan gum with lake color systems and plasticizer in aqueous film coating systems.

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EXAMPLE 12 - Gellan gum coating on vitamin tablets and placebos

Purpose: To apply clear coating of Gellan gum solution to colored vitamin tablets to demonstrate that acceptable gloss can be obtained.

5

Method: Using a 1.5% Gellan solution:

1500 grams total:

%	Grams
1.5% Gellan Gum	22.5 grams
10 0.10% Sodium Citrate**	1.5 grams
98.4% Deionized Water	1476 grams

**Dihydrate, powder

Mixing Instructions: Follow procedure recited in Example 1.

15

Coating Instructions: Follow procedure recited in Example 4 (sprayed at room temperature).

20 Tablets used totaled 420 grams (210 grams peach colored vitamins and 210 grams of uncoated placebo tablets)

25 In this Example, acceptable tablets were also produced which result in vitamin tablets and placebo tablets that had a high gloss and lubricious mouthfeel. This Example demonstrates that gellan gum applied as a clear aqueous coating in accordance with this invention is compatible with vitamins and placebo tablets and results in tablets having an improved gloss and mouthfeel over the uncoated tablets.

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EXAMPLE 13 - Gellan gum coating on vitamin tablets and placebos sprayed at 40°C

Purpose: To apply clear coating of Gellan gum solution to colored vitamin tablets to determine if appropriate gloss can be obtained.

5

Method: Using a 1.5% Gellan solution:

1500 grams total:

	%	Grams
	1.5% Gellan Gum (Ex 8096*)	22.5 grams
10	0.10% Sodium Citrate**	1.5 grams
	98.4% Deionized Water	1470.0 grams

**Dihydrate, powder

Mixing Instructions: Follow procedure recited in Example 1.

15

Coating Instructions: Follow procedure recited in Example 1 (sprayed at 40°C).

Tablets used totaled 420 grams (210 grams peach colored vitamins and 210 grams of uncoated placebo tablets)

20

In this Example, acceptable coated tablets were produced in accordance with this invention which had high gloss and lubricious mouthfeel comparable to the tablets from Example 13. This Example demonstrates that ability of gellan gum to be processed in accordance with this invention at elevated temperatures with no negative impact on gloss or mouthfeel of the coated tablets.

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EXAMPLE 14 - Gellan gum with pigment: Lake with PEG 400 increased*

*Rather than 20% PEG 400 of total gellan gum solids, 50% PEG 400 of gellan solids will be evaluated

5 Gellan solution preparation: Follow procedure recited in Example 1.

Mixing instructions: Follow procedure recited in Example 1.

Coating Preparation:

10 600 grams 1.5% Gellan solution (heated to 40°C)
 4.5 grams Peach (SS-1094)
 4.5 grams PEG 400

15 Peach (SS-1094) (40% solids)
 37.2% titanium dioxide 37.2 grams
 2.65% FD&C yellow no. 6 low dye lake
 0.15% red iron oxide 0.15 grams
 2.0% EDTA solution (40%) 2.00 grams
 58.0% distilled water 58.00 grams

20 Coating trial: (5-71-74-2) Spray 581.5 grams of above formula (40°C) onto 420 grams placebos using a fluidized column (similar in concept to an Aeromatic Strea 1). Samples of tablets taken at 0.5, 1.0, 1.5, 2.05 weight gains.

25 This resulted in improved and acceptable film flexibility, improved gloss and good tablet coverage. This Example results in acceptable tablets with high gloss and lubricious mouthfeel. This Example demonstrates the compatibility of gellan gum with lake color systems and plasticizer at elevated concentrations. The elevated plasticizer level enables greater film flexibility.

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EXAMPLE 15 - Gellan gum with pigment: white formula

*Gellan solution preparation: Used 1000 grams from solution made above, which had cooled to around 40°C.

5

Coating preparation:

1000 grams 1.5% gellan solution

9.4 grams White (SS-1031) (50% solids)

3.0 grams Propylene Glycol

10

3.0 grams Lecithin (Alcolec F-100)

White (SS-1031) (50%) solids

25% titanium dioxide 50 grams

25% talc 50 grams

15

2.5% EDTA solution (40%) 5 grams

47.5% distilled water 95 grams

Weigh gellan solution into appropriate beaker (37.5°C). Add Propylene Glycol and lecithin. Stir, with an appropriate stirrer until it is mixed well. Add white dispersion.

20

Keep temperature around 40°C prior to spraying. Combined at this temperature, pigment dispersed easily and mixed into the gellan solution with no problems..

25

Coating trial: Spray 711.2 grams of above formula (40°C) 420 grams placebos* using a fluidized column (similar in concept to Aeromatic Strea 1). Samples of tablets taken at 0.5, 1.0, 1.5, 2.0, 2.5, 3.0% weight gains.

*25 grams active tablets part of charge

The Example produced acceptable tablets that had good lubricious mouthfeel and gloss characteristics that are higher than commercially available white coating systems. This

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Example demonstrates that gellan gum is compatible with titanium based color systems and plasticizers. This Example also demonstrates gellan gum's ability to impart gloss in the presence of these ingredients.

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EXAMPLE 16 - Gellan gum with pigment: lake (with HPMC addition)

Using 1.5% gellan solution prepared above.

Coating preparation:

1000 grams 1.5% gellan solution

5 7.5 grams Green (SS-1091)

3.0 grams Hydroxypropylmethylcellose (Pharmacoat 606)

3.0 grams PEG 400

where PEG = polyethylene glycol 400 and

Green (SS-1091) comprised:

10	38.4% titanium dioxide	76.8 grams
	2.65% FD&C yellow No. 6 low dye lake	2.65 grams
	0.15% red iron oxide	0.15 grams
	2.0% EDTA solution (40%)	2.00 grams
	58.0% distilled water	58.00 grams for a total of 200 grams

15

Weigh gellan solution into appropriate beaker and heat. Add PEG 400 and HPMC (temperature when added =60°C). Mix with an appropriate stirrer until dissolved. Add lake dispersion until it is mixed well.

20 Coating trial: Spray 760.1 grams of above formula (40°C) 420 grams placebos* using a fluidized column (similar in concept to an Aeromatic Strea 1). Samples of tablets taken at 0.5, 1.0, 1.5, 2.0, 2.5, 3.0% weight gains.

*25 grams active tablets as part of charge (charge is the tablets to be coated which are provided to the fluidized column)

25

Results: Tablets coated to a 3% weight gain; addition of HPMC improved film flexibility and enabled formulae to be made with PEG added at a standard level (20% of gellan solids level); gloss was not compromised and is close to that which was obtained in tests using gellan with lecithin and PG. This Example further resulted in acceptable tablets with a higher gloss than tablets coated with HPMC alone. Also, the tablets of this Example prepared in accordance with this invention, had the lubricious mouthfeel

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**characteristic of gellan gum coatings. Further, this Example demonstated the
compatiblitiy of gellan gum with HPMC.**

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EXAMPLE 17 - Use of a side vented coating pan as a successful application system

A:

24" pan Accela Cotta 16 Kg. charge color coated

1.5% gellan gum, pan RPM 13

5 Process air Vol. 440CFM

T = 72°C (Inlet)

Exhaust air temperature 50-52°C

Two 1/4 Jau Tips 40100 liq cap. (0.040 inch internal diameters, 0.100 inch external diameter from Spray Systems)

10 134255-45 Air cap.

Atomizing Pressure 24-25 PSI

Feed Rate 55-70g/min

B:

15	60" Pan Acela Coata	successful coating	Charge 350 KG
	Process	Color Coat	Gelan Gum Coat
	Air Volume	5500 cfm	5500 cfm
	Temperature	70° F	75° F (Inlet)
	Exhaust T	47	52
20	Spray Rate	1200 g/m	1200 g/min
	Solids	12 %	1.5 %
	Atomizing Air	40 psi	25 psi

25 The Example provided acceptable tablets with high gloss and lubricious mouthfeel. This Example demonstrates the ability of gellan gum aqueous film coating system of this invention to be operated and scaled up from bench top equipment to a commercial size equipment.

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EXAMPLE 18 - Gellan gum coating solution with dye dispersion

A tablet coating composition comprised of a gellan gum composition was first prepared (1.5% gellan concentration) according to Example 1. Tablets (420 grams) were coated using a fluidized column (similar in concept to an Aeromatic Strea 1). These tablets were coated with a polymer/color coating composition and the gell gum solution which were combined as follows:

- 1000 grams 1.5% gellan solution
10 3.75 grams Green dye dispersion (D412)
3.0 grams Propylene Glycol
3.0 grams Lecithin (Alcolec F-100)

15 Weigh the gellan into a beaker and add the propylene glycol and lecithin while gellan preparation in +40°C. Once the propylene glycol and lecithin are dispersed, add the dye dispersion.

20 807.8 grams of above formula were sprayed onto 420 grams of tablets (395 grams of placebos and 25 grams of tablets with active drug substance).

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Run	Time	Weight	Inlet Temp°F	Exhaust Temp°F	Pump Setting	Comp Setting	Heater/ Blower	
							H	B
5	0	5.5	175	123	2.2	32		
	8:00	89.5	187	126	2.3	32	9	5.3
	15:00	181.5	190	124	2.5	32		
	23:00	287.0	190	123	2.5	32		
	30:00	381.5	190	123	2.5	32		
	35:00	450.0	191	123	2.5	32		
	45:00	593.0	191	124	2.5	32		
	60:00	787.5	191	125	2.5	32		
10	61:45	812.5	192	126	2.5	32		

This Example provided acceptable tablets with very high gloss and lubricious mouthfeel.
 This Example further demonstrates the compatibility of gellan gum with dye color systems and plasticizer.

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Thus, it is apparent that there has been provided, in accordance with the instant invention, a process that fully satisfies the objects and advantages set forth herein above. While the invention has been described with respect to various specific examples and embodiments thereof, it is understood that the invention is not limited thereto and many alternatives, modifications and variations will be apparent to those skilled in the art in light of the foregoing description. Accordingly, it is intended to embrace all such alternatives, modifications and variations as fall within the spirit and broad scope of the invention.

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WHAT IS CLAIMED IS:

1. A tablet coating comprising gellan gum.
- 5 2. The tablet coating of claim 1 wherein said gellan gum is present in an amount from about 0.025% to about 10% by weight of the total tablet.
3. The tablet coating of claims 1 or 2 wherein said gellan gum is present in an amount from about 0.05% to about 5% by weight of the total tablet.
- 10 4. The tablet coating of claims 1, 2 or 3 wherein said gellan gum is present in an amount from about 0.075% to about 3% by weight of the total tablet.
5. The tablet coating of claims 1, 2 or 3 wherein said coating further comprises a color.
- 15 6. The tablet coating of claims 1, 2 or 3 wherein said coating further comprises a plasticizer, or a surfactant.
- 20 7. The tablet coating of claims 1, 2 or 3 wherein said coating comprises gellan gum and is the primary coating.
8. The tablet coating of claim 1 where said coating comprises a polymer other than gellan gum as the primary coating and gellan gum is the secondary coating.
- 25 9. The tablet coating of claim 1 wherein said coating comprises gellan gum and is the only coating.

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10. The tablet coating of claim 1 wherein said primary coating comprises gellan gum and a color and said secondary coating comprises gellan gum.
- 5 11. A tablet coating having a high level of gloss comprising gellan gum wherein said gloss is characterized as about 200 to about 400 when characterization is done using a surface system analyzer.
- 10 12. The tablet coating of claim 11 wherein said level of gloss is from about 250 to about 350.
13. The tablet coating of claim 11 wherein said level of gloss is from about 200 to about 400 and further comprises a color.
- 15 14. An active drug coated with gellan gum.
15. The active drug of claim 14 wherein said drug is coated with gellan gum in a primary or secondary coating.
- 20 16. The active drug of claim 14 wherein said drug is coated with gellan gum in a primary coating.
17. The active drug of claim 14 wherein said drug is coated with gellan gum in one coating.
- 25 18. The active drug of claim 14 wherein said tablet coating further comprises a color.
19. The active drug of claim 14 wherein said tablet coating further comprises a plasticizer or a surfactant.

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20. The active drug of claim 14 wherein said tablet coating further comprises an active ingredient.
- 5 21. A process for preparing a coated tablet which process comprises the steps:
 - a. admixing gellan gum and water under shear to prepare an aqueous gellan gum coating composition useful for coating tablets and
 - b. applying said aqueous coating composition in an adherent fashion to a tablet whereby said coated tablet is formed and (optionally) drying said tablet to form said coated tablet.
- 10 22. The process of claim 21 wherein said aqueous gellan gum coating composition is applied once or more than once to a tablet.
- 15 23. The process of claim 21 wherein said aqueous coating composition comprises a color.
- 20 24. The process of claim 21 wherein a coating of a polymer other than gellan gum is applied to said tablet prior to application thereof of said aqueous gellan gum coating composition.
- 25 25. The process of claim 24 which said polymer is in combination with gellan gum.
26. The process of claim 21 wherein more than one coating is applied to a tablet and said coating is selected from the group consisting of gellan gum and another polymer.
27. The process of claim 21 wherein said tablet of claim 19(a) is coated or uncoated.

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28. The process of claim 21 wherein said applying is carried out by applying said aqueous gellan gum composition by mechanical means whereby said aqueous composition is directed to said tablet to be coated.
5
29. The process of claim 28 wherein said mechanical means comprises spraying.
30. The process of claim 28 wherein said aqueous gellan gum composition is applied to a coated tablet by spraying said aqueous composition onto said coated tablet to form a tablet containing an additional coating.
10
31. The process of claim 28 wherein said mechanical means comprises use of a spray nozzle.
32. The process of claim 31 wherein said nozzle has a nozzle throat diameter from about 0.028 to about 0.100 inch.
15
33. The process of claim 21 wherein said process is carried out in a fluidized bed.
34. The process of claim 21 wherein said fluidized bed is in a "Wurster" type tower.
20
35. The process of claim 21 wherein said application is carried out in a side vented coating pan.
36. The process of claim 21 wherein said admixing of step (a) is carried out under conditions of effective shear.
25
37. The process of claim 28 wherein said high aqueous gellan gum composition has a viscosity from about 44 cps to about 55,000 cps.

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38. The process of claim 37 wherein said viscosity is from about 2,200 to about 50,000 cps.
- 5 39. The process of claim 21 wherein said gellan gum is present from about 0.1% to about 10% by weight in said aqueous coating composition.
40. The process of claim 39 wherein said gellan gum is present from about 0.25% to about 5% by weight in said aqueous coating composition.
- 10 41. The process of claim 46 wherein said gellan gum is present from about 0.075% to about 3% by weight in said aqueous coating composition.
42. A gellan gum product suitable for forming coated tablets comprising gellan gum in an amount of about 0.1% to about 10% and having a viscosity of about 15 44 cps to about 55,000 cps prior to application.
43. The gellan gum product of claim 42 wherein said gellan gum is present in an amount from about 0.25% to about 5% weight.
- 20 44. The gellan gum product of claim 43 wherein said gellan gum is present in an amount from about 0.075% to about 3% weight.
45. The gellan gum product of claim 42 wherein said coating comprises an active 25 ingredient.
46. The gellan gum product of claim 42 wherein said coating comprises a plasticizer.
47. A placebo coated with an effective amount of gellan gum.

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48. The active drug of claim 14, wherein the gloss of said active drug is higher than that of a similar drug absent a gellan gum coating.
- 5 49. A tablet coated with gellan gum, a color and a plasticizer.
50. A tablet coated with an effective amount of gellan gum.
51. An active drug in coated tablet form produced by the process of claim 21.
- 10 52. The active drug of claim 14 produced by the process of claim 22.
53. The active drug of claim 14 produced by the process of claim 23.
- 15 54. The active drug of claim 14 produced by the process of claim 24.
55. The active drug of claim 14 produced by the process of claim 25.
56. The active drug of claim 14 produced by the process of claim 26.
- 20 57. The active drug of claim 14 produced by the process of claim 27.
58. The active drug of claim 14 produced by the process of claim 28.
- 25 59. The tablet of claim 46 wherein said coating is a partial coating.
60. The tablet of claim 1 wherein said coating comprises gellan gum and aspartame.
61. The tablet of claim 1 wherein said coating comprises gellan gum and one or more

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selected from the group consisting of sugar, gellan gum calcium, sorbitol, mannitol, maltose, maltitol, xylitol and mixtures thereof.

- 5 62. The tablet of claim 1 wherein said coating comprises gellan gum, another polymer and sugar.
- 10 63. A method of treating a patient (or animal) which comprises administering to said patient a therapeutically effective amount of a coated tablet, wherein said coated tablet comprises a tablet coated with gellan gum and said tablet further comprises a therapeutically effective amount of a therapeutically effective drug beneficial to said patient.
- 15 64. The method of claim 63 wherein said coated tablet comprises gellan gum which is present in an amount from about 0.025% to about 10% of the total tablet weight and wherein such treatment is oral or rectal.
- 20 65. The method of claim 64 wherein said gellan gum is present in an amount from about 0.05% to about 5% of the total tablet weight.
- 25 66. The method of claim 65 wherein said gellan gum is present in an amount from about 0.075% to about 3% of the total tablet weight.
- 30 67. The method of claim 63 wherein said coating further comprises a color.
- 35 68. The method of claim 63 wherein said coating further comprises a plasticizer.
- 40 69. The method of claim 63 wherein said coating comprises gellan gum and is the primary coating.

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70. The method of claim 63 wherein said coating comprises a polymer other than gellan gum as the primary coating and gellan gum is the secondary coating.
- 5 71. The method of claim 63 wherein said coating comprises gellan gum and is the only coating.
72. The method of claim 63 wherein said primary coating comprises gellan gum and a color and said secondary coating comprises gellan gum.
- 10 73. The method of claim 63 wherein said tablet coating has a high level of gloss comprising gellan gum wherein said gloss is from about 200 to about 400.
74. The method of claim 63 wherein said level of gloss is from about 250 to about 350.
- 15 75. The method of claim 63 wherein said level of gloss is from about 200 to about 400 and further comprises a color.
76. The method of claim 63 wherein said level of gloss is higher than said gloss would be absent a gellan gum coating.
- 20 77. A tablet coating composition comprising gellan gum in an effective amount which is prepared by admixing gellan gum and water under effective shear to prepare an aqueous gellan gum coating composition useful for coating tablets.
- 25 78. The tablet coating composition of claim 77 wherein said amount of gellan gum is from about 0.025% to about 10% by weight.

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79. The tablet coating composition of claim 78 wherein said amount of said gellan gum is from about 0.05% to about 5% by weight.
80. The tablet coating composition of claim 79 wherein said amount of said gellan gum is from about 0.075% to about 3% by weight.
5
81. The tablet coating composition of claim 72 wherein the viscosity of said aqueous gellan gum coating composition is from about 44 to about 55,000 cps prior to application to a tablet.
10
82. The tablet coating composition of claim 81 wherein said viscosity is from about 2,200 to about 50,000 cps prior to application to a tablet.
83. The tablet coating composition of claim 72 wherein said amount of gellan gum is from about 0.025% to about 10% by weight.
15
84. The tablet coating composition of claim 83 wherein said amount of gellan gum is from about 0.05% to about 5% by weight.
85. The tablet coating composition of claim 84 wherein said amount of gellan gum is from about 0.075% to about 3% by weight.
20
86. The active drug of claim 12 having one or more enhanced properties selected from the group selected from higher gloss, better mouthfeel, non-tackiness, being swallowable with little or no or reduced accompanying liquid and little taste.
25
87. The active drug of claims 1, 50 or 62 wherein said drug possesses an enhanced property which comprises better swallowability as compared to a tablet absent a gellan gum coating.

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88. The tablet composition of claim 1 wherein said tablet composition comprises gellan gum and is prepared by the process of claim 19(a).
89. The tablet composition of claim 81 wherein said tablet composition comprises gellan gum in an amount from about 0.025% to about 10% by weight.

5

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/23430

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K47/36 A61K9/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 048 123 A (MERCK & CO INC) 24 March 1982 see the whole document see examples 4,5 ---	1-10, 14-36, 39-58, 61-72, 76-81, 83-89
A	US 4 326 052 A (KANG KENNETH S ET AL) 20 April 1982 cited in the application ---	
A	US 4 385 123 A (KANG KENNETH S ET AL) 24 May 1983 cited in the application ---	
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

2 March 1999

10/03/1999

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Authorized officer

Fischer, W

INTERNATIONAL SEARCH REPORTInt'l. Jpnal Application No
PCT/US 98/23430**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 630 580 A (MERCK & CO INC) 28 December 1994 -----	
A	US 5 334 640 A (DESAI NEIL P ET AL) 2 August 1994 -----	

INTERNATIONAL SEARCH REPORT

...ernational application No.

PCT/US 98/23430

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 63-76
because they relate to subject matter not required to be searched by this Authority, namely:
See FURTHER INFORMATION Sheet PCT/ISA/210

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Although claims 63-76 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Claims Nos.: 63-76

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

 International Application No
 PCT/US 98/23430

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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